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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/753,078	01/08/2004	David H. Reifsnyder	12441.00050/16331.004	6550

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EXAMINER	
ROOKE, AGNES BEATA	
ART UNIT	**PAPER NUMBER**
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/753,078	REIFSNYDER ET AL.	
	Examiner	Art Unit	
	Agnes B. Rooke	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-54* is/are pending in the application.

4a) Of the above claim(s) *20-49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19 and 50-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/ are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/23/2007 has been entered.

The amendments to the claims filed on 12/23/2007 have been acknowledged.

Status of Claims

Claims 1-54 are pending. Claims 20-49 are withdrawn. New claims 50-54 are added. Thus, claims 1-19 and 50-54 are pending and under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-19 and 50-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 10, and 19 contain the trademark/trade name ISOQUANT®. Where a trademark or trade name is used in a claim as a limitation to identify or describe a

particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe Promega ISOQUANT® kit and, accordingly, the identification/description is indefinite. All dependent claims are included in this rejection because they do not further define the trademark product being claimed.

Claims 1-19 and new claims 50-54 are indefinite because the phrase "less than about 12%" does not specify the exact value that is being claimed, since the value can be less than 12% or it can be about 12%, where about 12% is not necessary less than 12%. Therefore, the claims are indefinite.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 10, and 19, are amended to include the phrase "at least 200 grams." Applicants' state that the support for the amendment is in the specification on page 8, paragraph 30. Examiner, concludes that the phrase "at least 200 grams" in reference to the TFPI inhibitor or TFPI analog molecules does not have support in the specification because the numerical values in regards to the TFPI are specified in the disclosure, however, the value of "at least 200 grams" do not have an upper limit and thus the value is open ended and indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-19 and new claims 50-54 are rejected under 35 U.S.C. 102(b) as being anticipated by EP 0 559 632.

EP 0 559 632 teaches a purified preparation and pharmaceutical compositions comprising a plurality of tissue factor pathway inhibitor (TFPI) molecules. Absent evidence to the contrary, it appears that the preparation is patentably indistinguishable from that of the present claims.

EP 0 559 632 teaches that a TFPI preparation refolded and purified by the method disclosed therein was greater than 95% homogeneous suggesting that there was minimal misfolding, aggregation, carbamylation, oxidation, deamidation, or cysteine

adducts. There is also no evidence or indication that the preparation contains TFPI polypeptides that have cysteine adducts or are misfolded, aggregated, carbamylated, oxidized, or deamidated.

The EP 0 559 632 publication teaches a purified preparation and pharmaceutical compositions comprising a plurality of tissue factor pathway inhibitor (TFPI) molecules including Ala-TFPI (p. 8, lines 44-52). Absent evidence to the contrary, it appears that the preparation is patentably indistinguishable from that of the present claims. The EP 0 559 632 teaches that a TFPI preparation refolded and purified by the method disclosed therein was greater than 95% homogeneous suggesting that there was minimal misfolding, aggregation, carbamylation, oxidation, deamidation, or cysteine adducts. There is also no evidence or indication that the preparation of the EP 0 559 632 contains TFPI polypeptides that have cysteine adducts or are misfolded, aggregated, carbamylated, oxidized, or deamidated.

Applicants responded that claims do not read on all compositions having less than about 12% of any one type of modified species. However, Applicants also state that it is true that a preparation with less than 12% oxidized species and less than about 12% total oxidized species meets the limitations of the claims. Further, Applicants state that the claims are amended to recite large scale preparation comprising at least 200 grams of TFPI or TFPI analog and that those analogs are highly purified.

Examiner acknowledges Applicants arguments however finds them unpersuasive since by amending the claims to include at least 200 grams of TFPI or TFPI analog does not change the fact that still less than about 12% of the TFPI or TFPI analog

molecules are modified. Thus, by increasing the numerical value of TFPI in "grams" does not change the required "percentage" since the percentage is the limiting factor in the claims as presented.

Further, Applicants discuss a commercial scale preparation of the TFPI where the particular steps in the purification process are specified.

Examiner acknowledges Applicants' argument however finds it unpersuasive because the instant issue regards a composition of TFPI and not the method of making/producing of such composition.

Moreover, Applicants distinguish the EP 0 559 632 by stating that it possess different steps and different purification methods that produce TFPI, and that the prior art teaches only preparation of 500 mg of TFPI protein, and that EP 0 559 632 nowhere suggest the commercial quantities of TFPI being at least 200 grams, which are claimed in the instant invention.

Examiner acknowledges Applicants' arguments however finds it unpersuasive because the 500 mg of TFPI taught by EP 0 559 632 is still in the range of "at least 200 mg." Second, a composition of the TFPI is instantly examined, and not the method of producing such a composition. Further, new claims 53 and 54 refer to the amounts of TFPI as being in the range of 600-900 grams and 800-1200 grams respectively. Examiner includes those claims in the instant rejection because the increase of the amount of the composition, here TFPI, would not change the characteristics of the invention or its function since still "less than about 12%" of the TFPI that is modified is a limitation.

Therefore, the claims stand rejected as being anticipated by EP 0 559 632. All previous arguments presented by the examiner support the rejection but are not rehearsed in the instant office action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0 559 632 view of U.S. 6,525,102.

EP 0 559 632 teaches a purified preparation and pharmaceutical compositions comprising a plurality of tissue factor pathway inhibitor (TFPI) molecules including Ala-TFPI (p. 8, lines 44-52). Absent evidence to the contrary, it appears that the preparation is patentably indistinguishable from that of the present claims.

EP 0 559 632 teaches that a TFPI preparation refolded and purified by the method disclosed therein was greater than 95% homogeneous suggesting that there was minimal misfolding, aggregation, carbamylation, oxidation, deamidation, or cysteine adducts.

There is also no evidence or indication that the preparation of the EP 0 559 632 contains TFPI polypeptides that have cysteine adducts or are misfolded, aggregated, carbamylated, oxidized, or deamidated. The office does not have the facilities for

examining and comparing Applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See Ex parte Phillips, 28 USPQ 1302, 1303 (BPAI 1993), In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray, 10 USPQ2d 1922, 1923 (BPAI 1989). Thus, absent evidence to the contrary, it appears that the preparation of the '632 publication is patentably indistinguishable from that of the present claims.

EP 0 559 632 does not teach that the pharmaceutical compositions comprise 20mM sodium citrate, 300 mM L-arginine, and 5 mM methionine, pH 5.5.

However, the US 6,525,102 teaches a preparation comprising TFPI in sodium citrate buffer (Col. 3, lines 41-45) and that adding arginine to a TFPI preparation protects TFPI from aggregation (Col. 6, lines 8-55).

The U.S. 6,525,102 teaches that methionine can be added to TFPI preparations to protect the polypeptide against oxidation (Col. 10, lines 21-43).

Therefore, it would have been obvious to one of ordinary skill in the art to modify the pharmaceutical composition comprising TFPI produced in the EP 0 559 632 to contain sodium citrate, L-arginine, and methionine as taught in the U.S. 6,525,102 patent. The EP 0 559 632 teaches a TFPI product that is patentably indistinguishable from that of the claims in its homogeneity. One of ordinary skill in the art would be motivated to add L-arginine and methionine to the pharmaceutical preparation of the EP

0 559 632 in order to preserve that homogeneity by preventing aggregation and oxidation during storage. The U.S. 6,525,102 patent teaches that it is well within the skill in the art to determine the concentration of these agents (Col. 8, lines 27-30). It was also well within the art to determine sodium citrate concentration that would buffer the acidity of L-arginine and lead to greater TFPI stability (a goal of the U.S. 6,525,102 patent). Thus, one would have been motivated to combine the teachings of the U.S. 6,525,102 patent and the EP 0 559 632 to optimize the TFPI stability after expression and purification.

Applicants responded that EP 0 559 632 does not teach large scale preparation formulation comprising at least 200 grams of ala-TFPI as recited in claim 19.

Examiner responds that EP 0 559 632 teaches pharmaceutical compositions comprising plurality of TFPI including ala-TFPI (see page 8, lines 44-52). Therefore, as stated by Applicants on page 17, 3rd paragraph, line 1, of the Remarks, EP 0 559 632 teaches 500 mg of TFPI protein that is purified by cation exchange chromatography and thus includes the ala-TFPI in the amount of at least 200 grams.

Therefore, the claims stand rejected as being unpatentable over EP 0 559 632 view of U.S. 6,525,102 because of the aforementioned arguments. Also, all previous arguments presented by the examiner support the rejection but are not rehearsed in the instant office action.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Agnes Rooke whose telephone number is 571-272-2055. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-272-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

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KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER